REMARKS

Claims 1-77 and 113-140 are pending. Claims 27-35, 48-77 and 113-140 are withdrawn as directed to nonelected subject matter. Claims 6, 8, 10, 12-26, 42-44, 46 and 47 read on the elected species; claims 1-5, 7, 9, 11, 36-41 and 45 are withdrawn as directed to unelected species. Claims 1, 2, 5, and 6 are amended. The amended claims are supported in the specification by, for example, paragraph [0029]. Note that applicants' summary of the disposition of claims differs from that of the Office.

Examiner Interview

Applicants thank the Examiner for the courtesy of a telephonic interview on March 27, 2007 during which applicants' attorneys, Janet S. Hendrickson and Kathleen M. Petrillo and Examiners Angela J. Martin and Raymond Alejandro discussed the art of record, namely Gregg et al. (U.S. Patent No. 5,264,105) and Yamamoto et al. (U.S. Patent Application Publication No. 2002/0127440). Examiner Martin stated that the 35 U.S.C. § 103 rejection made in the October 10, 2006 Office action would be removed, but 35 U.S.C. § 102 rejections based on Gregg et al. and Yamamoto et al. would be presented in the next Office action. The examiner further stated that if amendments to claim 6, part (c) were made with respect to the catalytic activation, the amendment may overcome the 102 rejection based on Gregg et al. and if amendments were made to claim 6, part (b) with respect to releasing electrons, the amendment may overcome the 102 rejection based on Yamamoto et al.

The Claimed Invention

In this case, claim 6 requires the elements of (1) an electron conductor, (2) an enzyme capable of reacting with an oxidized form of an electron mediator and a fuel fluid to produce an oxidized form of the fuel fluid and a reduced form of the electron mediator, (3) the reduced form of the electron mediator being capable of releasing electrons to the electron conductor, (4) an enzyme immobilization material immobilizing and stabilizing the enzyme, (5) the enzyme immobilization material being permeable to the fuel fluid, and (6) the stabilized enzyme retaining at least about 75% of its initial catalytic activity for at least about 30 days.

35 U.S.C. § 102 Rejections

An anticipating reference must disclose all of the elements of the claims.

Gregg et al.

Reconsideration is respectfully requested of the rejection of claims 6, 12-18, 23, 25, and 42-44 as being anticipated by Gregg et al. (U.S. Patent No. 5,264,105). The Office asserts that Gregg et al. teach a bioanode "comprising (a) an electron conductor; (b) at least one enzyme capable of reacting with an oxidized form of an electron mediator and a fuel fluid to produce an oxidized form of the fuel fluid and a reduced form of the electron mediator, the reduced form of the electron mediator being capable of releasing electrons to the electron conductor; and (c) an enzyme immobilization material comprising the electron mediator, the enzyme immobilization material being capable of immobilizing and stabilizing the enzyme, the material being permeable to the fuel fluid."[1]

Gregg et al. generally disclose enzyme electrodes that contain a three-dimensional redox polymer network that has bound redox enzymes for use in amperometric biosensors. Although Gregg et al. describe enzymes that are immobilized within redox polymers, the reference is silent on the stability of these enzymes within the electrodes. Thus, the Gregg et al. reference does not explicitly disclose the requirement of enzyme stabilization by the enzyme immobilization material providing a stabilized enzyme retaining at least about 75% of its initial catalytic activity for at least about 30 days.

As noted in M.P.E.P. §2112.IV, a rejection based upon the inherency of a claimed element must be supported by evidence that the missing element is necessarily present in the reference:

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is

[1] See Office action dated April 3, 2007 at page 2.

> necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). . . .
>
> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original) (Applicant's invention was directed to a biaxially oriented, flexible dilation catheter balloon (a tube which expands upon inflation) used, for example, in clearing the blood vessels of heart patients). The examiner applied a U.S. patent to Schjeldahl which disclosed injection molding a tubular preform and then injecting air into the preform to expand it against a mold (blow molding). The reference did not directly state that the end product balloon was biaxially oriented. It did disclose that the balloon was "formed from a thin flexible inelastic, high tensile strength, biaxially oriented synthetic plastic material." *Id.* at 1462 (emphasis in original). The examiner argued that Schjeldahl's balloon was inherently biaxially oriented. The Board reversed on the basis that the examiner did not provide objective evidence or cogent technical reasoning to support the conclusion of inherency.).

Applicants respectfully submit that the present rejection is not supported by objective evidence or cogent technical reasoning to support the conclusion of inherency with regard to enzyme stability. Absent such evidence or reasoning, anticipation has not been established and the burden of proof has not shifted to the applicant to prove that the alleged inherent enzyme stability is not necessarily present in the cited reference.

In the interest of advancing prosecution of this application, applicants provide the following evidence that the enzyme stability is not necessarily present in the cited references. Applicants refer to a later publication by one of the same inventors of the Gregg et al. electrode (Adam Heller of the University of Texas, Austin; referenced as Ohara et al.), which describes a lactate electrode including a redox polymer of $Os(dimethylbipyridine)_2Cl$ complexed with poly(1-vinylimidazole) with a Nafion® overcoating as retaining 50% of its initial catalytic activity upon continuous use for about 7.4 days when operating at a concentration of 2 mM lactate at 22°C.[2] The electrodes

[2] See Ohara et al., *Anal. Chem.* **1994**, *66*, 2451-2457 at page 2457 and Table 3.

described by Ohara et al. are similar to the electrodes described by Gregg et al. and differ primarily in the ligands attached to the Os center of the redox polymer. More specifically, the redox polymer of Ohara et al., as shown in FIG. 1 of that reference and as reproduced below, is Os(dimethylbipyridine)$_2$Cl complexed with poly(1-vinylimidazole) (or PVI-Os(dimethylbpy)$_2$Cl):

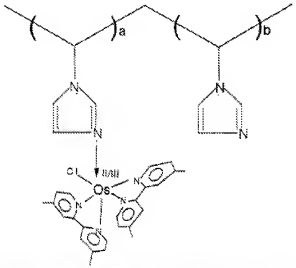

Figure 1. Chemical structure of Os(4,4'-dimethylbpy)$_2$Cl complexed with poly(1-vinylimidazole).

The redox polymer of Gregg et al., as shown in FIG. 3 of that reference and as reproduced below, is Os(bipyridine)$_2$Cl complexed with poly(1-vinylimidazole) (or PVI-Os(bpy)$_2$Cl):

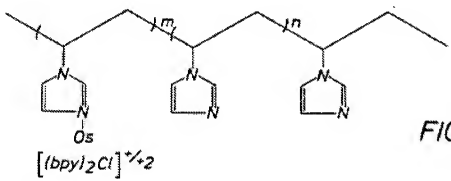

FIG. 3

In other words, the Ohara et al. polymer has methyl groups on the bipyridine ring and the Gregg et al. polymer does not. Ohara et al. varied the ligands attached to Os during the five years following the priority date of Gregg et al. to lower the redox potential of the redox polymer, thus, improving the electron transfer through the redox polymer. Since these later improved redox polymers only provided an enzyme stability wherein 50% of

the initial catalytic activity was retained for 7.4 days, applicants submit that a skilled person would not have a reasonable expectation that the Gregg et al. electrodes would have a stabilized enzyme as required by claim 6, which retains at least about 75% of its initial catalytic activity for at least about 30 days.

Additionally, claim 12 depends on claim 6 and further requires the enzyme immobilization material comprise a modified perfluoro sulfonic acid-PTFE copolymer. While Gregg et al. disclose a perfluoro sulfonic acid-PTFE copolymer, it is not a modified perfluoro sulfonic acid-PTFE copolymer. The instant specification describes the modified perfluoro sulfonic acid-PTFE copolymer as a perfluorinated ion exchange polymer membrane that is modified with a hydrophobic cation that is larger than the ammonium (NH_4^+) ion.[3] In contrast, Gregg et al. disclose that the electrode was dip coated in a solution of Nafion® to overcoat the electrode.[4] The Nafion® layer described by Gregg et al. is not modified with a hydrophobic cation. Thus, Gregg et al. do not disclose, nor contemplate an enzyme immobilization material comprising a modified perfluoro sulfonic acid-PTFE copolymer. Thus, claims 6 and 12 are not anticipated by Gregg et al. under 35 U.S.C. § 102.

Further, claims 13-18, 23, 25, and 42-44 depend from claim 6, incorporate all the elements of claim 6 and are not anticipated by Gregg et al. for the reasons described above for claim 6.

Yamamoto et al.

Reconsideration is respectfully requested of the rejection of claims 6, 13-16, 24, and 26 as being anticipated by Yamamoto et al. (U.S. Patent Application Publication No. 2002/0127440). The Office asserts that Yamamoto et al. teach a bioanode "comprising (a) an electron conductor (0031); (b) at least one enzyme (0029) capable of reacting with an oxidized form of an electron mediator and a fuel fluid to produce an oxidized form of the fuel fluid and a reduced form of the electron mediator, the reduced form of the electron mediator being capable of releasing electrons to the electron conductor; and (c) an enzyme immobilization material comprising the electron mediator,

[3] See specification at paragraph [0041].
[4] U.S. Patent No. 5,264,105, column 10, lines 5-21.

the enzyme immobilization material being capable of immobilizing and stabilizing the enzyme, the material being permeable to the fuel fluid (0032)."[5]

Yamamoto et al. generally disclose polymer electrolyte fuel cells containing an anode and a cathode containing platinum wherein oxidation of hydrogen to water occurs at the anode and reduction of oxygen to water occurs at the cathode. Yamamoto et al. also describe a fuel supply path that includes a biochemical catalyst that generally produces hydrogen from an organic fuel that is subsequently used as a fuel in a conventional hydrogen fuel cell.

Although Yamamoto et al. describe biochemical catalysts that are enzymes, the reference is silent on the stability of these enzymes within the fuel supply path. Thus, the Yamamoto et al. reference does not explicitly disclose the requirement of a stabilized enzyme retaining at least about 75% of its initial catalytic activity for at least about 30 days. Further, the electron mediator (e.g., NADH) disclosed by Yamamoto et al. does not meet the requirement of claim 6 that the reduced form of the electron mediator be capable of releasing electrons to the electron conductor. NADH could transfer electrons to an electrocatalyst that in turn could release electrons to the electron conductor, but NADH cannot release electrons directly to the electron conductor as required by claim 6. Yamamoto does not disclose nor contemplate the use of an electrocatalyst to transfer electrons from the electron mediator to the electron conductor because Yamamoto's biocatalyst is used to produce hydrogen that is used as a fuel source for a conventional fuel cell. Thus, claim 6, and the claims that depend therefrom are not anticipated by Yamamoto et al.

35 U.S.C. § 103 Rejection

Reconsideration is respectfully requested of the rejection under 35 U.S.C. § 103 of claims 6, 8, 10, 19-22, 46, and 47 as being unpatentable over Gregg et al. (U.S. Patent No. 5,264,105) in view of Saini et al. (U.S. Patent No. 5,521,101). The Office asserts that Gregg et al. teach a bioanode as described above and Saini et al. teach "an electrode comprising an electron mediator comprising potassium ferrocyanide," a "quaternary ammonium cation wherein R1-R4 are butyl or ethyl," and an electron

[5] See Office action dated April 3, 2007 at page 3.

conductor that comprises "modified perfluorosulfonic acid-PTFE (Nafion) copolymer."[6] The Office further asserts that it would have been obvious for a person of ordinary skill to "modify Gregg's Nafion with tertbutyl ammonium ion and enzyme-Nafion compositions, as taught by Saini, for the benefit of eliminating acid groups and increasing the robustness of the immobilizing materials."[7]

As described in more detail above, claim 6 requires an enzyme immobilization material that provides a stabilized enzyme retaining at least about 75% of its initial catalytic activity for at least about 30 days. The deficiencies of the Gregg et al. reference with respect to the enzyme stability element of claim 6 and the modified perfluorosulfonic acid-PTFE copolymer are described above. Saini et al. generally disclose sensors for monitoring analytes in the gaseous phase. The disclosure of Saini et al. does not remedy the deficiencies of Gregg et al. The enzyme immobilization materials described by Saini et al. do not meet the enzyme stabilization requirement of claim 6. For example, when Nafion® was used as the enzyme immobilization material, Saini et al. describe the results as follows:

> Enzyme-Nafion modified electrodes were only biocatalytically active for approximately 30 minutes. The enzyme was presumed to be inactivated by the acidic groups of the Nafion polymer and/or excessive dehydration.[8]

By way of further example, when ionically conducting gels of tetrabutylammonium toluene-4-sulfonate were used as the enzyme immobilization material, Saini et al. describes the enzyme as having limited stability since the "enzyme proved to be relatively stable for a number of hours within the gel matrix."[9] Thus, the enzymes immobilized at electrodes described by Saini et al. were stable for only a number of hours, whereas claim 6 and the claims that depend therefrom require the enzyme to retain at least about 75% of its initial catalytic activity for at least about 30 days.

Further, as described in more detail above, claim 10 includes all the elements of claim 6 and further requires the enzyme immobilization material be an alkylammonium salt extracted perfluoro sulfonic acid-PTFE copolymer. In contrast, Saini et al. disclose use of Nafion® (a perfluoro sulfonic acid-PTFE copolymer). Thus, the Saini et al.

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[6] See Office action dated April 3, 2007 at page 4.
[7] See Office action dated April 3, 2007 at page 4-5.
[8] U.S. Patent No. 5,521,101 at column 12, lines 14-17.
[9] U.S. Patent No. 5,521,101 at column 13, lines 38-39.

disclosure does not disclose or suggest enzyme immobilization materials that meet the enzyme stability requirement, and it also does not disclose, nor contemplate use of an alkylammonium salt extracted perfluoro sulfonic acid-PTFE copolymer.

In particular, with the disclosure of Saini et al. that the enzyme immobilization materials provide enzymes retaining catalytic activity for only several hours, a person skilled in the art would not have been led to modify the electrodes of Saini et al. and Gregg et al. to arrive at the claimed bioanodes. Due to this inferior enzyme stability data, the disclosure of Gregg et al. alone or in combination with the Saini et al. disclosure would have led away from using Nafion® as an enzyme immobilization material and also would not have provided a reasonable expectation that electrodes containing Nafion® enzyme immobilization materials would have provided the enzyme stability required by the claimed bioanodes.

Contrary to the Office's assertion, neither Gregg et al. nor Saini et al. suggest use of an alkylammonium salt extracted perfluoro sulfonic acid-PTFE copolymer as an enzyme immobilization material as required by claim 10. While Saini et al. disclose tetrabutylammonium and tetraethylammonium salts along with Nafion® polymers as electrolyte matrices, these ammonium salts do not modify the Nafion® polymers. Moreover, persons of ordinary skill would not have contemplated modifying these Nafion® polymers to form an alkylammonium salt extracted perfluoro sulfonic acid-PTFE copolymer given that Saini et al.'s Nafion® enzyme immobilization material allowed the enzyme to retain its catalytic activity for only 30 minutes.

Moreover, Saini et al. did not use Nafion® polymers in combination with tetrabutyl or tetraethyl ammonium salts, but substituted them for the ammonium salts. The Office provides no rationale why a person of ordinary skill upon reading Saini et al. would have contemplated that substitution of the acid groups of the Nafion® polymers by such ammonium salts would have provided increased robustness. Saini et al. do not disclose or suggest modified Nafion® as described by the instant specification and would not have led a skilled person to modify the Nafion® polymers for the benefit of eliminating acid groups and increasing the robustness of the immobilization material as the Office suggests. Thus, claims 6, 8, 10, 19-22, 46, and 47 are patentable under 35 U.S.C. § 103.

Rejoinder

Pursuant to M.P.E.P. §821.04, Applicants again request rejoinder of withdrawn claims 27-35, 49-52, 60-62, 114, and 117-130 as they depend from claim 6 and therefore require all the limitations of claim 6. Applicants further request reconsideration of withdrawn unelected species claims 1-5, 7, 9, 11, 36-41, and 45 because they either require all the limitations of claim 6 or overlap the scope of claim 6.

CONCLUSION

Applicant submits that the present application is now in condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,

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